CLAIMS

1. A method for preparing a humanized or human chimeric monoclonal antibody, with high effector activity, characterized in that it comprises the following steps:

a) producing and purifying monoclonal antibodies obtained from different sources, notably from cells, plants or non-human animals, possibly either genetically modified or transformed,

b) measuring the fucose content and the galactose content of the glycanic structures borne by the glycosylation site of the Fc region of said antibodies,

c) selecting antibodies for which the fucose content/galactose content ratio is less than or equal 0.6, preferentially 0.5 or 0.4.

2. The method according to claim 1, characterized in that said antibodies are produced in genetically modified cells by introducing at least one vector allowing the expression of said antibodies, said cells being eukaryotic or prokaryotic cells, notably cells from mammals, insects, plants, bacteria or yeasts.

3. The method according to any of claims 1 or 2, characterized in that said cells are genetically modified by introducing at least one vector allowing the expression of at least one polypeptide having a glycosyl transferase activity.

4. The method according to claim 3, characterized in that said glycosyl transferase activity is a galactosyl transferase activity.

5. The method according to claim 4, characterized in that said galactosyl transferase activity is a beta(1,4)-galactosyl transferase activity or a beta(1,3)-galactosyl transferase activity;

6. The method according to any of the preceding claims, characterized in that said cells have an activity relating to the synthesis and/or the transport of GDP-fucose and/or to the activity of an enzyme involved in adding fucose to the oligosaccharide of the glycosylation site of the antibodies, either reduced or deleted.

7. The method according to claim 6, characterized in that the enzyme involved in the synthesis of GDP-fucose is GMD (GDP-D-mannose 4,6-dehydratase), Fx (GDP-keto-6-deoximannose 3,5-epimerase, 4-reductase) or GFPP (GDP-beta-L-fucose pyrophosphorylase).

8. The method according to claim 6, characterized in that said enzyme involved in adding fucose is a fucosyl transferase.

9. The method according to any of the preceding claims, characterized in that, if in step b), the measured ratio is larger than 0.6, a defucosylation is performed and/or galactose residues are added to said antibody before step c).

10. The method according to the preceding claim, characterized in that said defucosylation is performed by adding a fucosidase in the medium containing the antibody.

11. The method according to any of claims 8 or 9, characterized in that the addition of galactose residues is performed by adding a galactosyl transferase in the medium containing the antibody.

12. The method according to any of the preceding claims, characterized in that said cells stem from animal or human cell lines, said lines being notably selected notably from lines of rat myelomas notably YB2/0 and IR983F, of human myeloma such as Namalwa or any other cell of human origin such

as PERC6, CHO lines, notably CHO-K, CHO-Lec10, CHO-Lec1, CHO Pro-5, CHO dhfr-, CHO Lec13 lines or other lines selected from Wil-2, Jurkat, Vero, Molt-4, COS-7, 293-HEK, BHK, K6H6, NSO, SP2/0-Ag 14 and P3X63Ag8.653.

13. The method according to any of the preceding claims, characterized in that said antibody is an IgG type human immunoglobulin.

14. The preparation method according to any of the preceding claims, characterized in that the antibody is an anti-Rhesus factor (anti-D), anti-CD, anti-tumors, anti-virus, anti-CD20 or anti-HLA-DR.

15. The method according to any of the preceding claims, characterized in that said effector activity is a ADCC type functional activity.

16. A method for increasing the effector activity of a composition of immunologically functional molecules, comprising the increase in galactose content and/or reduction in fucose content of the composition of molecules.

17. The method according claim 16, characterized in that said immunological functional molecules are monoclonal or polyclonal antibodies.

18. The method according to any claims 16 or 17, characterized in that said molecules have high fucose content in the native condition.

19. The method according to any claims 16 to 18, characterized in that the reduction in fucose content is due to a defucosylation of said composition through the action of a fucosidase, notably an α,1,6 fucosidase.

20. The method according to any claims 16 to 19, characterized in that the increase in galactose content of said composition is due to a galactosylation of the composition through the action of a galactosyl transferase.

21. A cell derived from the YB2/0 cell line, in which at least one vector coding for an antibody molecule is introduced, said cell producing an antibody for which the fucose content/galactose content ratio of the oligosaccharides of the glycosylation site of the Fc region of the antibodies is less than or equal to 0.6.

22. The cell according to claims 21, characterized in that it is transfected with an expression vector coding for a galactosyl transferase.

23. The cell according to any of claims 21 or 22, characterized in that said galactosyl transferase is a beta(1,4)-galactosyl transferase or a beta(1,3)-galactosyl transferase.

24. The cell according to any of claims 21 to 23, characterized in that said cell overexpresses said galactosyl transferase.

25. The cell according to any of claims 21 to 24, characterized in that said galactosyl transferase is coded by a sequence originating from humans, mice, hamsters, cows, sheep, goats, pigs, horses, rats, monkeys, rabbits or chickens.

26. The cell according to claim 25, characterized in that said sequence is the NM 001497, AB 024434, NM 003780, BC 053006, XM 242992, or NM 177512 sequence.

27. A method for preparing antibodies for which the glycanic structures borne by the glycosylation site of the Fc

region has a fucose content/galactose content ratio less than or equal to 0.6, preferentially less than 0.5 or even 0.4, comprising the culture of a cell according to any of claims 21 to 26 in a culture medium and under conditions allowing expression of said vectors.

28. Therapeutic antibodies having high effector activity capable of being obtained from the method according to any of claims 1 to 20 and 27, said antibodies being characterized in that they have on their glycosylation site of the Fc region, glycanic structures having a fucose content/galactose content ratio less than 0.6, preferentially less than 0.5 or even 0.4.

29. A pharmaceutical composition comprising an antibody according to claim 28 and at least one excipient.

30. A pharmaceutical composition comprising at least 50%, preferentially 60%, 70%, 80% or even 90% or 99% of a monoclonal antibody for which the glycanic structures borne by the glycosylation site of the Fc region have a fucose content/galactose content ratio less than 0.6, preferentially less than 0.5 or even 0.4.

31. The pharmaceutical composition according to any of claims 29 or 30, wherein the antibody is directed against a non-ubiquitous normal antigen, notably a Rhesus factor, such as the Rhesus factor (D) of the human red corpuscle, or an antigen of a pathological cell or on a pathogenic organism for humans, in particular against an antigen of a cancer cell.

32. The pharmaceutical composition according to any of claims 29 to 31, characterized in that said antibodies are IgGs.

33. The use of an antibody according to claim 28 for preparing a drug intended for treating allo-immunization, notably the hemolytic disease of the newborn child.

34. The use of an antibody according to claim 28 for preparing a drug intended for treating auto-immune diseases, cancers and infections by pathogenic agents, notably for treating diseases selected from Sezary's syndrome, solid cancers, notably for which the antigenic targets are weakly expressed, notably breast cancer, pathologies related to the environment notably affecting persons exposed to polychlorinated biphenyls, infectious diseases, notably tuberculosis, chronic fatigue syndrome (CFS), parasite infections such as schistosomulas, and viral infections.

35. The use of an antibody according to claim 28 for preparing a drug intended for treating cancers of positive class II HLA cells, acute lymphoid leukemias of B- and T-cells, acute and chronic myeloid leukemias, Burkitt's lymphoma, Hodgkin's lymphoma, myeloid leukemias, T-cell lymphomas, and non-Hodgkinian lymphomas.

36. The use according to any of claims 33 to 35 characterized in that the antibody is an anti-HLA-DR or an anti-CD20.

37. The use of an antibody according to claim 28 for manufacturing a drug intended to induce expression of IL-1α, IL-1β, Il-2, IL-3, IL-4, IL-5, IL-6, IL-12, IL-18, IL-21, TGFβ1, TGFβ2, TNFα, TNFβ, IFBγ, and IP10 by natural effector cells of the immune system, said drug being notably useful for treating cancer and viral, bacterial or parasite infections.

38. The use of an antibody according to claim 28 for manufacturing a drug intended for treating patients having one of the polymorphisms of CD16, in particular V/F158 or F/F158, notably patients in a condition of therapeutic failure with the presently available antibodies or subject to undesirable secondary effects.

39. A method for preparing a human or humanized chimeric monoclonal antibody having low effector activity, characterized in that it comprises the following steps:

a) producing and purifying monoclonal antibodies obtained from different sources, notably from cells, plants, or non-human animals, possibly either genetically modified or transformed,

b) measuring the fucose content and the galactose content of the glycanic structures borne by the glycosylation site of the Fc region of said antibodies,

c) selecting antibodies for which the fucose content/galactose content ratio is larger than 0.6.

40. The method according to claim 39, characterized in that said antibodies are produced in genetically modified cells by introducing at least one vector allowing expression of said antibodies, said cells being eukaryotic or prokaryotic cells, notably cells from mammals, insects, plants, bacteria, or yeasts.

41. The method according to any of claims 39 or 40, characterized in that said cells are genetically modified by introducing at least one vector allowing expression of at least one polypeptide having a glycosyl transferase activity.

42. The method according to claim 41 characterized in that said glycosyl transferase activity is a fucosyl transferase activity, notably an α1,6-fucosyl transferase activity.

43. The method according to any of claims 39 to 42, characterized in that said cells have an activity relating to the synthesis and/or the transport of UDP-galactose and/or to the activity of an enzyme involved in adding galactose to the oligosaccharide of the glycosylation site of the antibodies, either reduced or deleted.

44. The method according to claim 43, characterized in that said enzyme involved in the addition of galactose is a galactosyl transferase, notably a β 1,4-galactosyl transferase.

45. The method according to any of claims 39 to 44, characterized in that, if in step b), the measured ratio is less than 0.6, fucosylation is performed, and/or galactose residues are removed from said antibody before step c).

46. The method according to claim 45, characterized in that said degalactosylation is performed by adding a galactosidase in the medium containing the antibody.

47. The method according to any of claims 45 or 46, characterized in that addition of fucose residues is performed by adding a fucosyl transferase in the medium containing the antibody.

48. The method according to any of claims 39 to 47, characterized in that said antibody is an IgG type human immunoglobulin.

49. The preparation method according to any of claims 39 to 48, characterized in that the antibody is directed against a CD, a differentiation marker of human blood cells or against a pathogenic agent or its toxins, listed as being particularly dangerous in the case of bioterrorism, notably *Bacillus anthracis, Clostridium botulium, Yersinia pestis, Variola major, Francisella tularensis*, filoviruses, arenaviruses, *Brucella species, Clostridium perfringens, Salmonella, E.coli, Shigella, Coxiella burnetti*, ricin toxin, *Rickettsia*, viral encephalitis viruses, *Vibrio cholerae* or hantavirus.

50. The method according to claims 39 to 49, characterized in that said effector activity is an ADCC type functional activity.

51. A method for reducing the activity of a composition of immunologically functional molecules, comprising the increase in the fucose content and/or the reduction in the galactose content of said composition.

52. The method according to claim 51, characterized in that said immunologically functional molecules are monoclonal or polyclonal antibodies.

53. The method according to any of claims 51 or 52, characterized in that the increase in the fucose content is due to fucosylation of said composition through the action of a fucosyl transferase.

54. The method according to any of claims 51 to 53, characterized in that the reduction in the galactose content of said composition is due to degalactosylation of the composition through the action of a galactosidase.

55. An antibody composition capable of being obtained from a method according to any of claims 39 to 54.

56. The use of the composition according to claim 55 for preparing a drug intended for treating and/or preventing auto-immune diseases, allo-immunizations, notably PTI, graft rejection, allergies, asthma, dermatites, urticarias, erythemas, or inflammatory diseases.

57. A method for controlling the activity of a composition of immunologically functional molecules, comprising the regulation of the fucose content/galactose content ratio of the oligosaccharides of the glycosylation site of the Fc region of the antibodies.